

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (previously presented): A method of parallel analysis of biological specimens, comprising:

- obtaining a plurality of donor specimens;
- placing each donor specimen in an assigned location in a recipient array;
- obtaining a plurality of substantial copies of the recipient array in a manner that each substantial copy contains a plurality of donor specimens that maintain their assigned locations;
- performing a biological analysis of each substantial copy; and
- comparing the results of the biological analysis in corresponding assigned locations of different substantial copies to determine if there are correlations between the results of the biological analysis at each assigned location.

Claim 2 (original): The method of claim 1, wherein the donor specimen is obtained by boring an elongated sample from the donor specimen, which is placed in the assigned location in the recipient array.

Claim 3 (original): The method of claim 1, wherein the donor specimen is from a tumor.

Claim 4 (original): The method of claim 1, wherein the donor specimen is from a population of cells.

Claim 5 (original): The method of claim 3, wherein the donor specimen is from a hematological or cytological preparation.

Claim 6 (currently amended): The method of claim 1, wherein placing the donor specimen in an assigned location in the recipient array comprises forming an elongated receptacle in a ~~donor~~ recipient block, obtaining an elongated donor specimen, and placing the

elongated donor specimen in the elongated receptacle of the recipient block, and obtaining a plurality of copies comprising sectioning the array transverse to the elongated donor specimen.

Claim 7 (previously presented): The method of claim 6, wherein the elongated donor specimen is placed in a receptacle having a cross-sectional size and shape complementary to a cross-sectional size and shape of the elongated donor specimen.

Claim 8 (previously presented): The method of claim 7, wherein forming the elongated receptacle comprises forming a cylindrical bore in the recipient block, and the donor specimen is obtained by boring a cylindrical tissue specimen from a donor block, wherein a diameter of the elongated receptacle is substantially the same as a diameter of the donor specimen.

Claim 9 (previously presented): The method of claim 1, further comprising associating a clinical characteristic with each assigned location in the recipient array.

Claim 10 (previously presented): The method of claim 1, wherein performing the biological analyses comprises performing a different biological analysis on each copy.

Claim 11 (previously presented): The method of claim 10, wherein the different biological analyses are selected from the group consisting of at least an immunological analysis and a nucleic acid hybridization.

Claim 12 (previously presented): The method of claim 10, further comprising determining whether there are correlations between clinical characteristics, associated with each assigned location, and the different biological analyses.

Claim 13 (currently amended): The method of claim 1, wherein the biological ~~sample~~ specimen is a tissue specimen or cellular preparation.

Claim 14 (previously presented): The method of claim 12, wherein the clinical characteristics are determined apart from performing the different biological analysis of each copy of the array; and

the characteristics are one or more of patient age, tumor grade, tumor size, node status, and receptor status.

Claim 15 (previously presented): The method of claim 1, wherein placing the specimen in an assigned location in the array comprises placing a sample in a corresponding position of multiple copies of an array.

Claim 16 (currently amended): A method of parallel analysis of substantially identical arrays of tissue specimens, comprising:

~~forming a donor block comprising a biological specimen embedded in embedding medium;~~

obtaining a plurality of elongated donor sample cores from ~~the~~ a biological specimen;  
boring receptacle cores from a recipient embedding medium to form an array of elongated receptacles;

placing the donor sample cores in the elongated receptacles at assigned locations in the array;

sectioning the recipient embedding medium transverse to the elongated receptacles to obtain a cross-section of the donor sample cores in the array, while maintaining the assigned locations in the array in consecutive cross-sections;

performing a different biological analysis of each cross-section; and

comparing a result of each biological analysis in corresponding assigned locations of different sections to determine if there are correlations between the results of the different biological analyses at each assigned location.

Claim 17 (previously presented): The method of claim 16, further comprising comparing the results of the different biological analyses at each assigned location to clinical information about the biological specimen at the assigned location.

Claim 18 (previously presented): The method of claim 17, wherein the biological specimen is a tissue specimen from a tumor.

Claim 19 (previously presented): The method of claim 17, wherein the biological analyses are selected from the group consisting of a histologic analysis, an immunologic analysis, and a nucleic acid hybridization analysis.

Claim 20 (previously presented): The method of claim 17, wherein the results of the different biological analyses are compared to clinical information obtained about a subject from whom the biological specimen was obtained.

Claim 21 (previously presented): The method of claim 16, further comprising aligning a thin tissue section above the donor block to identify an area of interest from which the donor sample core is taken.

Claim 22 (currently amended): The method of claim 16, wherein the elongated donor sample core is a substantially cylindrical core that has a diameter that is less than ~~about~~ 1 mm.

Claim 23 (canceled).

Claim 24 (previously presented): The method of claim 1, further comprising using a nucleic acid microarray to identify a biomarker to be used in a biological analysis on the recipient array.

Claim 25 (previously presented): The method of claim 24, wherein the nucleic acid microarray is a cDNA or oligonucleotide microarray.

Claim 26 (previously presented): The method of claim 25, wherein the biomarker is selected by a high throughput immunological or genetic analysis.

Claim 27 (previously presented): The method of claim 24, wherein the biomarker comprises a marker for gene expression.

Claim 28 (previously presented): The method of claim 26, wherein the biomarker comprises a structural or numerical alternation of a chromosome, chromosomal region, gene, gene fragment or locus, or a gene function alteration.

Claim 29 (previously presented): The method of claim 1, wherein comparing the results comprises determining if there is an alteration of a gene by examining a marker for protein expression or other gene alteration.

Claim 30 (previously presented): The method of claim 29, wherein the alteration of protein expression is determined by an immunologic analysis.

Claim 31 (previously presented): The method of claim 29, wherein the alteration is an overexpression of vimentin in renal cell carcinoma, or an overexpression of IGFBP2 in human prostate cancer, or an overexpression of PDGFB in breast, lung, colon, testicular, endometrial or bladder cancer.

Claim 32 (currently amended): A method of analyzing genetic changes or gene expression in a tissue specimen, comprising:

screening multiple genes in a biological specimen, with a nucleic acid array that detects which genes are abnormally expressed in the biological specimen; and

screening multiple biological specimens in a biological specimen array, with a nucleic acid probe to detect which genes are abnormally expressed in the biological specimens;

wherein the result of screening multiple genes is used to select the nucleic acid probe to screen the multiple biological specimens, or wherein the result of screening multiple ~~tissue~~ biological specimens is used to select the array that detects which genes are abnormally expressed.

Claim 33 (previously presented): The method of claim 32, wherein screening multiple genes comprises performing a high throughput genomic technique.

Claim 34 (previously presented): The method of claim 32, wherein the high throughput genomic technique is selected from the group of cDNA or genomic DNA sequencing, protein sequencing, RDA, differential display, subtractive hybridization, SAGE, hybridization based sequencing, and cDNA and oligonucleotide arrays.

Claim 35 (previously presented): The method of claim 32, wherein screening multiple genes to determine which genes are abnormally expressed comprises searching databases and other biomedical sources of information.

Claim 36 (previously presented): The method of claim 32, wherein screening the multiple genes comprises using a cDNA array to determine which genes are abnormally expressed.

Claim 37 (previously presented): The method of claim 32, wherein screening the multiple genes comprises providing a DNA array which is assayed for a gene amplification, deletion, mutation, polymorphism, methylation change or other alternation of gene structure or function, or a genetic or molecular marker that reflects this change.

Claim 38 (previously presented): The method of claim 37, wherein the DNA array is a microarray that contains target loci that undergo differential expression in cancer.

Claim 39 (previously presented): The method of claim 32, wherein screening multiple genes obtained from a single biological specimen comprises hybridizing nucleic acid molecules associated with a cell with the DNA array that contains target loci that undergo differential expression, and determining which target loci indicate differential expression of a gene in the cell.

Claim 40 (previously presented): The method of claim 39, further comprising selecting a target locus that undergoes differential expression, providing a probe that includes or is complementary to at least a portion of the target locus, and using the probe to screen the multiple biological specimens.

Claim 41 (previously presented): The method of claim 32, wherein the biological specimen is a tissue specimen.

Claim 42 (previously presented): The method of claim 41, wherein the tissue specimen is a tumor specimen.

Claim 43 (previously presented): The method of claim 1, further comprising analyzing the results of the biological analyses to:

- a. evaluate a reagent for disease diagnosis or treatment;
- b. identify a prognostic marker for a disease;
- c. prioritize targets for drug development;
- d. assess or select therapy for a disease type;
- e. find a biochemical target for medical therapy;
- f. determine the frequency of a target in pathological and normal physiological tissue;
- g. identify therapeutic targets that are expressed in pathological tissue relative to normal physiological tissue;
- h. compare the expression or presence of a target at the DNA, RNA and protein level; or
- i. identify, validate, and prioritize targets that are defined by utilizing bioinformatic analyses.

Claim 44 (previously presented): The method of claim 43, wherein evaluating a reagent for disease diagnosis or treatment comprises evaluating a reagent selected from the group of antibodies, genetic probes, and antisense molecules.

Claim 45 (previously presented): The method of claim 44, wherein evaluating a reagent for disease diagnosis or treatment comprises evaluating a reagent selected from the group of biological inhibitors, biological enhancers, or other biological modulators.

Claim 46 (previously presented): The method of claim 43, wherein identifying a prognostic marker for cancer comprises selecting a marker associated with a poor clinical outcome.

Claim 47 (previously presented): The method of claim 43, wherein selecting therapy for the subject comprises selecting an antineoplastic therapy that is associated with a particular biological analysis outcome.

Claim 48 (previously presented): The method of claim 47, wherein the particular biological analysis outcome is an oncogene amplification, deletion, translocation, mutation or other genetic rearrangement which is correlated with a clinical response to a particular therapy.

Claim 49 (previously presented): The method of claim 1, wherein the donor specimens are specimens from one or more tumors.

Claim 50 (previously presented): The method of claim 49, wherein the donor specimens are from breast cancer tumors.

Claim 51 (previously presented): The method of claim 49, wherein the donor specimens are specimens from a plurality of tumors all of the same organ or histologic type.

Claim 52 (previously presented): The method of claim 48, wherein the donor specimens are specimens from a plurality of tumors from different organs or tissue types.



Claim 53 (previously presented): A method of analyzing cellular specimens in a matrix, with the specimens positioned at predetermined known positions, such that when multiple copies of the matrix are provided, a two dimensional array of specimens is presented on each copy, with each specimen at a predetermined position in the matrix, and wherein each matrix has a third dimension so that when sequential copies of the matrix are provided, the specimens maintain a predetermined relationship in the array, the method comprising exposing sequential copies of the matrix to an agent which interacts with the specimens of the array, to identify those specimens which share a common biological property.

Claim 54 (previously presented): The method of claim 53, wherein the specimens are provided in an elongated form, and multiple copies of the matrix are made by cutting sections from a three dimensional array into predetermined sections, such that as sequential sections of the matrix are cut, the specimens maintain the predetermined relationship.

Claim 55 (previously presented): The method of claim 53, wherein the common biological property is a morphologic or molecular characteristic.

Claim 56 (previously presented): The method of claim 53, wherein the common biological property is a presence or absence, or altered level of expression, of a gene or protein, alteration of copy number, structure or function of a gene, genetic locus, chromosomal region or chromosome.

Claim 57 (previously presented): The method of claim 54, wherein the common biological property is a specific reaction with an antibody specific for a specimen of interest.

Claim 58 (currently amended): The method of claim 53, wherein the common biological property is correlated with ~~an other~~ another characteristic of the specimens.

Claim 59 (previously presented): The method of claim 58, wherein the other characteristic of the specimens includes clinical information about a subject from whom each specimen was taken.

Claim 60 (previously presented): The method of claim 59, wherein the clinical information includes one or more of clinical course, treatment response, histological type or grade, tumor stage, and age and sex of the subject from whom each specimen was taken.

Claim 61 (previously presented): The method of claim 53, wherein the cellular specimen is a tissue specimen.

Claim 62 (previously presented): The method of claim 53, wherein the cellular specimen is a cellular suspension.

Claim 63 (previously presented): The method of claim 62, wherein the specimen is a liquid cellular specimen that has been converted into a solid cellular specimen.

Claims 64-65 (canceled).

Claim 66 (previously presented): The method of claim 53, further comprising exposing a gene array to a candidate specimen, and selecting a candidate probe for the specimen array.

Claim 67 (previously presented): The method of claim 53, wherein the common biological property is her-2 status, and the method further comprises selecting a therapy based on her-2 status.

Claim 68 (previously presented): The method of claim 63, wherein the specimens comprise a tissue from a model or transgenic organism.

Claim 69 (previously presented): The method of claim 68, wherein the specimens comprise tissue from the model or transgenic organism at different stages of development.

Claim 70 (previously presented): The method of claim 53, wherein the specimens comprise animal, yeast or bacterial cells.

Claim 71 (previously presented): The method of claim 70, wherein the cells are in a liquid suspension which is applied to a surface of a support.

Claim 72 (previously presented): The method of claim 71, wherein the liquid suspension is from a body fluid.

Claim 73 (previously presented): The method of claim 72, wherein the body fluid is selected from the group of a needle aspiration, a cytology specimen, urine, and ascitic fluid.

Claim 74 (previously presented): The method of claim 70, wherein the cells comprise a sample of a liquid malignancy.

Claim 75 (previously presented): The method of claim 74, wherein the liquid malignancy comprises a hematological malignancy.

Claim 76 (previously presented): The method of claim 70, wherein the cells are from one or more cell lines.

Claim 77 (previously presented): The method of claim 53, wherein the specimens comprise specimens from one or more tumors at different stages of progression.

Claim 78 (previously presented): The method of claim 77, wherein the one or more tumors are prostate cancer tumors.

Claims 79-85 (canceled).

Claim 86 (previously presented): The method of claim 49, wherein the donor specimens are specimens from one or more tumors selected from the group of prostate and bladder cancer.

Claim 87 (previously presented): The method of claim 1, wherein the method does not destroy the morphology or cellular structure of the donor specimens.

Claim 88 (previously presented): A method of parallel analysis of biological specimens, comprising:

- obtaining a plurality of donor specimens;
- placing each donor specimen in an assigned location in a recipient array;
- obtaining a plurality of sections of the recipient array in a manner that each section contains a plurality of donor specimens that maintain their assigned locations;
- performing a biological analysis of each section; and
- comparing the results of the biological analysis in corresponding assigned locations of different sections to determine if there are correlations between the results of the biological analysis at each assigned location.

Claim 89 (previously presented): The method of claim 1, further comprising correlating additional information concerning the donor specimens with the biological analysis correlation, wherein the additional information is at least one of patient demographics, clinical tumor staging data, and patient follow-up data.

Claim 90 (previously presented): A method of analysis of biological specimens, comprising:

- forming at least one donor block comprising a biological specimen embedded in embedding medium;
- obtaining a plurality of elongated donor sample cores from the biological specimen;
- boring receptacle cores from a recipient embedding medium to form an array of elongated receptacles;
- placing the donor sample cores in the elongated receptacles at assigned locations in the array;
- sectioning the recipient embedding medium transverse to the elongated receptacles to obtain at least one cross-section of the donor sample cores in the array, while maintaining the assigned locations in the array in consecutive cross-sections;

performing a biological analysis of each cross-section; and  
analyzing the results of the biological analysis to determine the frequency of a substance of interest in the cross-sections of the donor sample cores.

Claim 91 (previously presented): The method of claim 1, further comprising obtaining the donor specimens from a predetermined morphologically defined region of a tumor.

Claim 92 (previously presented): The method of claim 1, further comprising obtaining the donor specimens from a predetermined cell structure.

Claim 93 (previously presented): The method of claim 21, wherein the area of interest comprises a morphologically defined region of a tumor.

Claim 94 (previously presented): The method of claim 21, wherein the area of interest comprises a cell structure.

Claim 95 (new): The method of claim 1, wherein at least a first biological analysis is performed on a first substantial copy of the recipient array, and at least a second biological analysis is performed on a second substantial copy of the recipient array, wherein the first biological analysis and the second biological analysis are different.

Claim 96 (new): The method of claim 16, wherein performing a different biological analysis of each cross-section comprises performing at least a first biological analysis of a first cross-section and at least a second biological analysis of a second cross-section.

Claim 97 (new): The method of claim 53, comprising exposing a first sequential copy of the matrix to a first agent, and exposing at least one second sequential copy of the matrix to at least one second agent, wherein the first agent and the second agent are different.

Claim 98 (new): The method of claim 2, wherein the elongated sample is a substantially cylindrical core that has a diameter that is less than 1 mm.

Claim 99 (new): The method of claim 2, wherein the elongated sample is a substantially cylindrical core that has a diameter of 0.3 to 2.0 mm and a length of 1 to 4 mm.

Claim 100 (new): The method of claim 16, wherein the elongated donor sample core is a substantially cylindrical core that has a diameter of 0.3 to 2 mm.

Claim 101 (new): The method of claim 1, further comprising preparing substantial copies of recipient arrays, and comparing the results of the biological analysis in the corresponding assigned locations of different substantial copies of recipient arrays to determine if there are correlations between the results of the biological analysis at each assigned location in each different recipient array.

Claim 102 (new): The method of claim 6, further comprising preparing substantial copies of recipient blocks, and comparing the results of the biological analysis in the corresponding assigned locations of different substantial copies of recipient blocks to determine if there are correlations between the results of the biological analysis at each assigned location in each different recipient block.